PTO/SB/08A (08-03)

LO GARCIA

Approved for use through 07/31/2006. OMB 0651-0031

U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

CAT Bubstitute for form 1449A/PTO

Cite No.

Examiner

Initials \*

## SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT BY **APPLICANT**

(use as many sheets as necessary)

Number

None

U.S. Patent Document

Kind Code

(if known)

Sheet of

	Complete if Known
Application Number	10/635,696
Filing Date	August 5, 2003
First Named Inventor	Rapin, et al.
Group Art Unit	1632-1654
Examiner Name	Unassigned MARCELA M WRDER
Attorney Docket Number	10945.105001 Neuro 100

3383682 2 **U.S. PATENT DOCUMENTS** Pages, Columns, Lines, **Date of Publication** Name of Patentee or Applicant of Cited Where Relevant of Cited Document Document Passages or Relevant MM-DD-YYYY Figures Appear

		<u>.</u>		FOREIGN	PATENT DOCUMENTS			
Examiner Initials * Cite No. 1		Kind Code <sup>2</sup> (if known)	Name of Patentee or Applicant of Cited Document	Date of Publication of Cited Document MM-DD-YYYY	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	Т6		
			None				д	<del>                                     </del>

	·	OTHER PRIOR ART - NON PATENT LITERATURE DOCUMENTS	
Examiner Initials *	Cite No. 1	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	т6
mmics	AA	FADEN, A.I., et al., "Effect of TRH analogs on neurologic recovery after experimental spinal trauma," <i>Neurology</i> , 35:1331-1334 (1985).	† <del>'</del> -
	AB	GESCHWIND, M., et al., "Detection of apoptotic or necrotic death in neuronal cells by morphological, biochemical, and molecular analysis," in <u>Apoptosis Techniques and Protocols</u> , J. Poirier, ed., 1997, pp. 13-31.	
	AC	GUILOFF, R.J., "Thyrotropin releasing hormone and motorneurone disease", Reviews in the Neurosciences, 1:201-219 (1987).	
	AD	KURTZ, A.F., "Praktische Diagnostik," in <u>Aktuelles Wissen Hoechst</u> , Alzheimer-Patienten erkennen und behandeln," Hoechst AG, publisher (Munich, Germany, 1995), 68-69. With partial translation.	partial
	AE	RAPIN, J.R., "Les nootropes: propriétés pharmacologiques du piracétam et indications thérapeutiques," La Lettre du Pharmacologue, 6(5):108-111 (1992). With partial translation.	partial
	AF	SARTI, G., et al., "TRH-analogues: A possible treatment for symptoms of dementia in elderly patients?", Archives of Gerontology and Geriatrics, 12:173-177 (1991).	
mmce	AG	SZIRTES, T., et al., "Synthesis of thyrotropin-releasing hormone analogues. 1. Complete dissociation of central nervous system effects from thyrotropin-releasing activity," J. Med. Chem. 27:741-745 (1984).	
			3383682_2

Examines M				
	M = 1	Date	a	1 1 1
Signature ////amle ///	11 Condio (1)	Conside		122/04
			-	10.007

\*EXAMINER: Initial if reference considered, whether or not citation (s/in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, U. S. Patent and Trademark Office, Washington, DC 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Assistant Commissioner for Patents, Washington, DC 20231.

<sup>&</sup>lt;sup>1</sup> Unique citation designation number. <sup>2</sup> See attached Kinds of U.S. Patent Documents. <sup>3</sup> Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). <sup>4</sup> For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. <sup>5</sup> Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. <sup>6</sup> Applicant is to place a check mark here if

Approved for use through 10/31/2002. OMB 0651-0031 U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

**→** ⊞

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number

	Substitute for for	orm 1449A/PTO					Complete if Known		
						Application Number	10/635,696	1	
$\Lambda$	INFORM					Filing Date	August 5, 2003	1	
/ 1		MENT BY	APPL	ICAN'	T	First Named Inventor	Rapin, et al.	1	
0	O NOT 28 TOTAL S				Group Art Unit	1632 /654	1		
\	Mo.	as many shee	ts as neces	ssary)		Examiner Name	Unassigned MARCELA M CORD	TRO GARUA	
N	Shapte 19	1	of		3	Attorney Docket Number	NEURO 100	1	

3354576 1

				U.S. PATENT DOCUMENTS		
Examiner Initials *	Cite No.	U.S. Patent D Number	Kind Code (if known)	Name of Patentee or Applicant of Cited Document	Date of Publication of Cited Document MM-DD-YYYY	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
MMC6	AA	5,212,158	A	VANDAI	05-18-1993	
1	AB	5,973,111	A	BEMIS, et al.	10-26-1999	
	AC	6,156,572	A	BELLAMKONDA, et al.	12-05-2000	
mmc6	AD	6,235,929	. B1	POWERS	05-22-2001	

				F	OREIGN	N PATENT DOCUMENTS	}		
Examiner Initials *		Cite No. 1	Office 3		nent (ind Code <sup>2</sup> (if known)	Name of Patentee or Applicant of Cited Document	Date of Publication of Cited Document MM-DD-YYYY	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T6
		AE	EP	0,316,218	<b>A</b> 1	INORGAN, S.A.	05-17-1989		
1		AF	EP	1,018,341	A	CALPIS Co., Ltd.	07-12-2000		
		AG	EP	1,231,279	<b>A</b> 1	CALPIS Co., Ltd.	08-14-2002		П
		AH	EP	0,446,706	A2, A3	MERCK PATENT GESELLSCHAFT	09-18-1991		
		AI	JР	04-005240 w/ PAJ abstract	A	TAISHO PHARMACEUT. Co.;	01-09-1992		
		AĴ	wo	88/09604	A2	MEDICIS Corp.	12-15-1988		
		AK	WO	92/11850	A2	CORTEX PHARMA; GA. TECH. RES. INST.	07-23-1992		
		AL	wo	96/41638	A1	SANOFI WINTHROP	12-27-1996		
		AM	WO	98/14202	Al	AUCKLAND UNISERVICES, Ltd.	04-09-1998		
		AN	wo	01/28578	A2, A3	WRAIR	04-26-2001		
		AO	WO	01/34828	A1	CALPIS Co. Ltd.	05-17-2001		
	$\prod$	AP	WO	01/68114	A1	MONSANTO Co. (US)	09-20-2001		$\Box$
		AQ	wo	02/062373	A2,A3	TELL PHARM. AG	08-15-2002		
mmi	6	AR	wo	02/062828	A2,A3	TELL PHARM. AG	08-15-2002	<del></del>	

Examiner Signature	Maula M Corders Garie	Date Considered	09/0022/04

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, U. S. Patent and Trademark Office, Washington, DC 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Assistant Commissioner for Patents, Washington, DC 20231.

<sup>\*</sup>EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

<sup>&</sup>lt;sup>1</sup> Unique citation designation number. <sup>2</sup> See attached Kinds of U.S. Patent Documents. <sup>3</sup> Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). <sup>4</sup> For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. <sup>5</sup> Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. <sup>6</sup> Applicant is to place a check mark here if English language Translation is attached.

PTO/SB/08A (08-00)
Approved for use through 10/31/2002. OMB 0651-0031
U.S. Patent and Trademark Office, U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid QMB control number.

ſ	Substitute fo	or form 1449A/PTO			Complete if Known		
ı	•			_	Application Number	10/635,696	
k	TIMEOR	MATION	DISCLO	SURE	Filing Date	August 5, 2003	
1	STAT	MENT BY	APPLI	CANT	First Named Inventor	Rapin, et al.	
<b>)</b>	N 2 8 2002 &	<u> </u>			Group Art Unit	1632	
×	Nr. Z	e as many she	ets as neces	sary)	Examiner Name	Unassigned	
J	Sheet	2	of	3	Attorney Docket Number	NEURO 100	

3354576\_1

		OTHER PRIOR ART - NON PATENT LITERATURE DOCUMENTS	
Examiner Initials *	Cite No. 1	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T <sup>6</sup>
MmcG	BA	BEYER, H., and WALTER, W., Handbook of Organic Chemistry, by S. Hirzel Verlag, Stuttgard (English translation of the 22 <sup>nd</sup> edition of Lehrbuch der Organischen Chemie) (1996), pp. 827-838.	
	BB	BLUNDELL, T.L., et al., "Knowledge-based protein modelling and design", Eur. J. Biochem., 172:513-520 (1988).	
	BC	CHESSEBEUF, M., et al., "Rat liver epithelial cell cultures in a serum-free medium: primary cultures and derived cell lines expressing differentiated functions", In Vitro, 20(10):780-795 (1984).	
	BD	CLARK, M.C., et al., "Validation of the general purpose Tripos 5.2 force field", J. Comp. Chem., 10(8):982-1012 (1999).	
	BE	DE POOTER, H., et al., "N-acylamino acids and peptides IV the synthesis of N-cinnamyl-, N-p.coumaryl- and N-caffeyl-glycine and -glycyl-L-phenylalanine", Bull. Soc. Chim. Belg., 85(9):647-656 (1976). XP008015013.	
	BF	FADEN, A.I., et al., "Novel TRH analog improves motor and cognitive recovery after traumatic brain injury in rodents", Amer. J. Physiology 277(4, pt. 2):R1196-R1204 (1999), Chem. Abstr. 132:31033 XP002207513, XP008014976.	
	BG	FADEN, A.I., et al., "Structure-activity relationships of TRH analogs in rat spinal cord injury", Brain Research, 448:287-293 (1988). XP008015202.	
	ВН	GASTEIGER, J., et al., "Iterative partial equalization of orbital electronegativity a rapid access to atomic charges", Tetrahedron, 36:3219-3238 (1980).	
	BI	HAGG, T., et al., "Delayed treatment with nerve growth factor reverses the apparent loss of cholinergic neurons after acute brain damage", Exp. Neurol., 101:303-312 (1988).	
	BJ	JONES, D.T., et al., "A new approach to protein fold recognition", Nature, 358:86-89 (July 1992).	
	BK	JONES, D.T., "Protein secondary structure prediction based on position-specific scoring matrices", J. Mol. Biol., 292(2):195-202 (1999).	
	BL	KANSY, M., et al. "Physicochemical High Throughput Screening: Parallel Artificial Membrane Permeation Assay in the Description of Passive Absorption Processes", J. Med. Chem., 41(7):1007-1010 (March 26, 1998).	
mnce	BM	KHUEBACHOVA, M., et al., "Mapping the C terminal epitope of the Alzheimer's disease specific antibody MN423", J. Immunol. Methods (Elsevier Amsterdam, NL) 262(1-2):205-215 (2002). XP004352190.	

|--|

<sup>\*</sup>EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

<sup>&</sup>lt;sup>1</sup> Unique citation designation number. <sup>2</sup> See attached Kinds of U.S. Patent Documents, <sup>3</sup> Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). <sup>4</sup> For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. <sup>5</sup> Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. <sup>8</sup> Applicant is to place a check mark here if English language Translation is attached.

Approved for use through 10/31/2002, OMB 0851-0031 U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

	Substitute for form 1	1449A/PTO			Complete if Known			
1,					Application Number	10/635,696		
K	<b>ANFORMA</b>				Filing Date	August 5, 2003		
/上)	STATEME	NT BY	APPLI	CANT	First Named Inventor	Rapin, et al.		
۳. ۲۱	N 28 7002 5			_	Group Art Unit	1632	-	
M i	<b></b>	many sheets	as neces	sary)	Examiner Name	Unassigned		
	Space a talk	3	of	. 3	Attorney Docket Number	NEURO 100		

3354576\_1

OTHER PRIOR ART - NON PATENT LITERATURE DOCUMENTS							
Examiner Cite No. 1		Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.					
MMLL CA		LASKOWSKI, R.A., et al., "PROCHECK: a program to check the stereochemical quality of protein structures", J. Appl. Cryst., 26:283-291 (1993).					
	СВ	LE PONCIN-LAFITTE, M., et al., "Sound-avoidance conditioning and a mathematical approach to the description of acquisition performance", Math. Biosciences, 59:249-268 (1982).					
	CC	LUCO, J.M., "Prediction of the brain-blood distribution of a large set of drugs from structurally derived descriptors using partial least-squares (PLS) modeling", J. Chem. Inf. Comput. Sci., 39 (2):396-404 (1999)					
	CD	PARNETTI, L., et al., "Posatirelin for the treatment of late-onset Alzheimer's disease: a double-blind multicentre study vs citicoline and ascorbic acid", Acta Neurol. Scand. 92:135-140 (1995).					
	CE	VARON, S., et al., "Nerve Growth Factor in CNS Repair", J. Neurotrama, 11(5) (1994)					
	CF	WANG, R., et al., "SCORE: A new empirical method for estimating the binding affinity of a protein-ligand complex", J. Mol. Model., 4:379-394 (1998).					
	CG	WEINER, S.J., et al., "A new force field for molecular mechanical simulation of nucleic acids and proteins", J. Am. Chem. Soc., 106:765-784 (1984)					
mmcb	СН	WIESMAN, C., et al., "Crystal structure of nerve growth factor in complex with the ligand-binding domain of the TrkA receptor", Nature, 401:184 (September 9, 1999).					

3354576\_1

Examiner Signature	Marle	M lodes	Game	Date Considered	09/22/04

<sup>\*</sup>EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

<sup>&</sup>lt;sup>1</sup> Unique citation designation number. <sup>2</sup> See attached Kinds of U.S. Patent Documents. <sup>3</sup> Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). <sup>4</sup> For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. <sup>5</sup> Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. <sup>6</sup> Applicant is to place a check mark here if English language Translation is attached.